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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/163,089	09/29/1998	IAN F. C. MCKENZIE	4102-1	9586

22442 7590 12/26/2002

SHERIDAN ROSS PC  
1560 BROADWAY  
SUITE 1200  
DENVER, CO 80202

EXAMINER
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ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 12/26/2002

27

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/163,089

Applicant(s)

MCKENZIE ET AL.

Examiner

Robert A. Zeman

Art Unit

1645

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 November 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☒ Applicant's reply has overcome the following rejection(s): see attached.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☒ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: NoneClaim(s) objected to: NoneClaim(s) rejected: 1,3-17,19-21,24-26,38 and 70.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
10. ☐ Other: \_\_\_\_\_

h28  
LYNETTE R. F. SMITH  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1-60

### **ADVISORY ACTION**

The amendment filed on 11-27-2002 is acknowledged. Claim 9 has been amended.

Claims 1, 3-17, 19-21, 22-26, 38 and 70 are pending.

The Declaration of Dr. Pietersz under 35 U.S.C. 1.132 filed on 11-27-2002 is acknowledged. However, said Declaration will not be considered since it was not fully executed. Applicant has indicated that a fully executed Declaration would be sent under separate cover. To date, a fully executed Declaration has not been received. It should also be noted that said declaration would not have been considered even if it had been perfected since it was not timely filed. Said Declaration, contrary to Applicant's assertion, deals with issues raised in rejections made prior to the Final rejection mailed on 7-29-2002.

### ***Claim Rejections Withdrawn***

The rejection of claim 9 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "induce mannose receptor" is withdrawn in light of the amendment thereto.

The rejection of claims 1, 3-17, 19-21, 24-26, 38 and 70 under 35 U.S.C. 103(a), as being unpatentable over Apostolopoulos et al. (PNAS Vol. 92, pages 10128-10132) in view of Koning et al. (WO 98/13378) is withdrawn. Applicant's arguments have been fully considered and deemed persuasive.

***Claim Rejections Maintained***

***35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 3-17, 19-21, 24-26, 38 and 70 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunoregulatory compositions comprising mannose receptor bearing cells, and a conjugate comprising MUC1 (antigen) and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes, does not reasonably provide enablement for immunoregulatory compositions comprising mannose bearing cells and a conjugate comprising any antigen and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized polymer comprising free aldehydes is maintained for reasons of record.

It should be noted that Applicant's arguments are predicated, in part, on a Declaration not made of record. Below Applicant's arguments will be addressed to the degree they read on the record.

**Applicant argues:**

1. Other antigens when conjugated to mannan induce an *in vivo* cellular immune response as shown in the Declaration by Dr. Pietersz (filed on 4-8-02) and the papers by Stambas et al.
2. The mannose receptor bearing cells are inherently involved in the cellular response.

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3. A T-cell response follows the exposure of antigen presenting cells (dendritic cells or macrophages) to the antigen.
4. The *in vivo* T cell response to the administration of non-MUC1 antigens conjugated to mannan is a true reflection of how the same antigen conjugates would behave after treatment with mannose receptor cells *ex vivo* i.e. demonstration that the conjugate works *in vivo* is sufficient to address the expectation of how conjugates will behave as an *ex vivo* composition.
5. The presence of at least one mannose unit in the antigen-carbohydrate polymer is sufficient to provide immunogenicity. Hence the presence of a single mannose unit in the carbohydrate polymer will enable that particular conjugate to bind to APCs and result in the presentation of the antigen by APCs *in vivo*.
6. The demonstration of operability of a conjugate comprising an antigen and an oxidized carbohydrate polymer comprising mannose enables the claimed invention.
7. The aim of the present invention is to efficiently induce (boost) a cellular response to antigens so that there is effective vaccination.
8. The newly submitted Declaration of Dr. Pietersz demonstrate the *in vivo* or *ex vivo* pulsing of dendritic cells with mannose antigen conjugates where the antigens are not MUC1 and the ability of pulsed APCs to induce cellular responses in animals.

Applicant's arguments have been fully considered and deemed non-persuasive. The instant invention is drawn to compositions comprising isolated mannose receptor-bearing cells **and** a conjugate comprising an antigen and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes. The

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mannose receptor-bearing cells are a required component of said composition. Applicant's arguments, as well as the papers by Stambas et al., demonstrate the effects of the antigen-polymer conjugate only. Since Applicant's arguments do not address compositions that fall within the metes and bounds of the rejected claims, they are deemed non-persuasive.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 608-7991. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Robert A. Zeman  
December 23, 2002

### **ADVISORY ACTION**

The amendment filed on 11-27-2002 is acknowledged. Claim 9 has been amended.

Claims 1, 3-17, 19-21, 22-26, 38 and 70 are pending.

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